REMARKS

Entry of the foregoing, reexamination and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested.

As correctly indicated in the Office Action, claims 1-21 are pending in this application. Applicants note with appreciation that priority under 35 U.S.C. § 119 has been acknowledged.

By the foregoing amendment, claims 1-3, 10, 12 and 18 have been amended and claims 13-14 deleted to further clarify Applicants' invention. Applicants reserve the right to pursue in a continuation or divisional application any subject matter canceled by way of this amendment.

Support for the amendments to the claims can be found in the claims as filed and throughout the specification, especially on page 2, line 20, page 4, lines 22-34 and Example 2, pages 15-16. Accordingly, no new matter has been added.

The Specification

The specification stands objected to for certain informalities. Specifically, the specification purportedly recites a sentence without a capital letter and recites a range without an upper range. The specification has been amended to remove the sentence on page 12, lines 3-4 which was objected to. The specification on page 5, line 31, has been amended to recite "0-0.8%" rather than "0.8 - 0% w/v", thus providing a proper range. Applicant submits hat this was a typographical error and

thus correcting it does not add new matter to the specification. However, in further support, Applicant notes that this concentration of ammonium chloride is merely an example of a solution that his hypotonic in relation to plasma, and refer the Examiner to page 5, lines 29-30 of the specification to support this assertion.

Objections to the Claims

Claims 1-3, 10 and 12-14 stand objected to for various informalities.

Specifically, claims 1-3, 10 and 12-14 stand objected to for the recitation of "lysation" and "in stead". Claims 1-2 and 12 have been amended to recite "lysis" and "instead". Claims 13-14 have been deleted by way of the present Amendment. Claim 10 has been amended to recite "(SIP)" after the full length phrase for which it is an abbreviation, rather than before.

Claims 2, 13-14, 18 and 20-21 stand objected to as being in improper dependent form for purportedly failing to limit the subject matter of a previous claim. As suggested by the Examiner, the preamble in step (a) of claims 1 and 12 has been amended herein to recite that the claimed process separates plasma from blood or from a buffy coat fraction. Thus, Applicants submit that this objection is obviated.

Claim 18 is objected to for the recitation of "semi-continuous", while base claim 12 recites an apparatus for continuous purification. Claim 18 has been amended herein to recite "continuous" rather than "semi-continuous".

Claims 13 and 14 are objected to for purportedly stating what is put into the apparatus rather than defining any structural limitations upon the apparatus. These claims have been deleted by way of the present Amendment.

Applicant submits that these objections have been obviated.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 1-21 stand rejected under 35 U.S.C. § 112, second paragraph, as purportedly indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claims 1 and 12 stand rejected for the recitation of "separate plasma from the blood by filtration in order to achieve a buffy coat fraction", because it purportedly appears from the specification that there would need to be an unrecited settling step prior to the filtration step of separating the plasma from the buffy coat. Applicants respectfully submit that according to the present invention, the plasma is separated from blood or from a buffy coat fraction via filtration. Thus, there is no unrecited step, and this rejection is moot.

Claims 2 and 13 stand rejected because they are purportedly confusing in relation to base claims 1 and 12. As discussed above, the preamble in step (a) of claims 1 and 12 has been amended herein to recite that the claimed process separates plasma from blood or from a buffy coat fraction. Thus, Applicants submit that this rejection is obviated.

Claims 1, 12 and 18 stand rejected for the purported recitation of "continuous" or "semi-continuous" in claim 18, but not in base claims 1 and 12.. Claim 18 has been amended herein to recite "continuous" rather than "semi-continuous". Thus, Applicants submit that this rejection is obviated.

Claim 10 stands rejected to for the recitation of "adapted for clear in place (CIP) cleaning and (SIP) sanitation in place." The Examiner asserts that claim 10 does not recite any positively cleaning or sanitizing steps. Claim 10 has been amended herein to specifically recite cleaning and sanitizing steps. Thus, Applicants submit that this rejection is obviated.

Claim 12 stands rejected as the Examiner asserts that it is confusing and non-idiomatic. As discussed above, the preamble of claim has been amended herein to more clearly recite the purpose of the claimed process. Claim 12 is further rejected for the recitation of "lysation" because it recites that lysation occurs in the mixer, while the specification purportedly teaches that lysation is achieved in the retention vessel. Claim 12 has been amended herein to recite that lysation occurs in the retention vessel. Thus, Applicants submit that this rejection is obviated.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 1, 3-12 and 14-19 stand rejected under 35 U.S.C. § 112, first paragraph, for purportedly containing subject matter which was not described in the specification in such a way to enable the skilled artisan to make and/or use the

invention. Specifically, the Office Action asserts that the application does not disclose a process or apparatus that enables "separating plasma from blood by filtration in order to achieve a filtered buffy coat fraction", as recited in step (a) of claims 1 and 12. The Office Action further asserts that the specification merely discloses that a settling step is necessary in order to provide a buffy coat fraction from the blood.

Applicant respectfully submits that the recitation of a process or apparatus that enables "separating plasma from blood by filtration in order to achieve a filtered buffy coat fraction", as recited in step (a) of claims 1 and 12, is enabled. For purposes of clarification, Applicant notes that this disclosure should be understood as a description of a "buffy coat" in general terms. Plasma is usually separated from blood by centrifugation, but according to the present invention, the plasma is separated from blood or from a buffy coat fraction via filtration. Specifically, a filtered buffy coat fraction is obtained. (See also p 4, lines 22-34, of the present specification). Further, Applicant submits that the present specification is enabling for filtration. Specifically, filtration parameters are discussed at p 5, lines 13-27 and further exemplified in Example 1 on p 7, line 9 - p 8, line 4 with reference to Fig 2.

Claims 12-19 stand rejected under 35 U.S.C. § 112, first paragraph, for purportedly containing subjected matter which was not described in the specification in such a way to enable the skilled artisan to make and/or use the invention.

Specifically, the Office Action asserts that the specification does not disclose a static mixer that enables lysation as recited in claim 12.

The test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed reasonably conveys to the skilled artisan that the inventor had possession of the invention at that time of the later claimed subject matter, rather than the presence or absence of literal support in the specification for the claim language. *See Ex parte Remark*, 15 USPQ2d 1498, 1506 (P.B.A.I. 1990).

Thus, Applicant submits that the specification does provide adequate written description regarding a static mixer for lysation. Specifically, Applicant respectfully emphasizes that while mixing of buffy coat and hypotonic solution occurs in the static mixer, the lysis occurs in the retention vessel. Thus, there is no need for a static mixer. Rather, the specification supplies the written description required in support of the lysation occurring in the retention vessel. Applicant refers the Examiner to Example 1, p 8, lines 13-17, of the present specification.

Thus, Applicant submits that the rejections under 35 U.S.C. § 112, first paragraph are obviated.

Rejections Under 35 U.S.C. § 102

Claims 1-11 and 20-21 stand rejected under 35 U.S.C. § 102(b) as purportedly anticipated by Jones *et al.* (U.S. Patent No. 4,294,824). The Examiner asserts that Jones *et al.* discloses the processes of claims 1-11.

For proving anticipation, "anticipation requires the presence in a single prior art disclosure of." Jamesbury Corp. v. Litton Industrial Products, Inc. 225 U.S.P.Q. 253, 256 (Fed. Cir. 1985). The cited reference does not describe or suggest all of the elements of the rejected claims, as discussed in greater detail below.

Applicant submits that Jones *et al.* do not disclose a process according to the invention. Specifically, the process of Jones *et al.* does not include an initial step, in which plasma is separated from blood or from a buffy coat fraction by filtration. In contrast, the process according to the presently claimed invention includes an initial step of separating plasma from blood or from a buffy coat fraction by filtration, as discussed in detail is the disclosure of the present invention.

Further, as noted by the Office Action, the steps of Jones *et al.* are carried out in a different order from those of the claimed invention. Applicant notes that because each step recited in the rejected claims following the initial step (a) recites the preceding step. Thus, there is can be no ambiguity regarding the order in which the steps are conducted, and Jones *et al.* fails to disclose all elements of a claimed invention as arranged in the claims.

Thus, Applicant submits that this rejection should be withdrawn.

CONCLUSION

Based on the foregoing, this application is believed to be in condition for allowance. A Notice to that effect is respectfully solicited. However, if any issues remain outstanding after consideration of this Amendment and Reply, the Examiner is respectfully requested to contact the undersigned so that prosecution may be expedited.

Respectfully submitted,

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Date: August 19, 2002

Attachment to Amendment and Reply dated August 19, 2002

Marked-Up Copy

Page 5, Paragraph Beginning at Line 28

In order to achieve lysation of the erythrocytes in buffy coat fraction, this fraction is mixed with a hypotonic solution in relation to plasma, e.g. aqueous ammonium chloride solution (e.g. 0 - 0.8% w/v) [(e.g. 0.8 - 0 % w/v)] or, preferably 0.8 %, but when using lower concentrations the lysation time has to be decreased. The flow of hypotonic solution is preferably twice the flow of the buffy coat fraction. Top ensure effective mixing, the mixture of the buffy coat fraction and e.g. the NH_4Cl solution is lead through a static mixer and further to a retention vessel. The retention vessel is designed in a manner, considering the flow/volume ration, that a retention time of about 0.5 - 10 minutes is achieved, depending on the kind of hypotonic solution and the temperature used, and that the solution becomes homogenous in the entire vessel. The retention vessel is designated in a manner that a retention time of preferably 5 - 10 minutes is achieved when ammonium chloride solution is used, most preferably 10 minutes if cold 0.8% ammonium chloride solution is used.

Page 11, Paragraph Beginning at Line 34

The results in Table 1 shows in average a better total yield with the inventive, Exp. cells in comparison with Ref.-cells. Since the two processes, Exp.-cell and

Ref.-cell started with the same amount of cells and the volume of the final concentrated leukocyte cell suspension is the same for both processes, it is possible to calculate the recovery of cells from each process. [get more cells from the exp.] When comparing the cell concentration in the trials performed 961121 and 961127 when the same amount of cell suspension have been added, it is obvious that the inventive process results in a higher cell recovery. Therefore, it is also possible to get more interferon from the inventive process since the yield and yield per cell is about the same.

Attachment to Amendment and Reply dated August 19, 2002

Marked-up Claims 1, 2, 10, 12, and 18

1. (Amended) Process for the separation of plasma from blood or from a buffy coat fraction [continuous purification and concentration of leukocytes from blood], characterized in that said process comprises the following steps:

(a) separating plasma from the blood by filtration in order to achieve a filtered buffy coat fraction;

(b) adding an aqueous solution, which is hypotonic in relation to plasma, to the buffy coat fraction from step (a), in order to achieve lysis [lysation] of erythrocytes contained in the buffy coat fraction;

(c) mixing the buffy coat fraction and the aqueous hypotonic solution from step (b) in a mixing device;

(d) leading the mixture from step (c) through a retention vessel;

(e) leading the mixture from step (d) through a centrifuge in order to separate the leukocytes;

(f) collecting the separated leukocytes from step (e).

2. (Amended) Process according to claim 1, characterized in that a buffy coat fraction, obtained from blood, is used instead [in stead] of blood in step (a) and plasma is removed from this buffy coat fraction by filtration.

10. (Twice Amended) Process according to claim 1, characterized in that the process is automatically operated and adapted for clean in place (CIP) cleaning and [(SIP)] sanitation in place (SIP), wherein

the CIP is performed by automatically cleaning a system at site by pumping cleaning solutions in the system; and

the SIP is performed by sanitizing a system at site by a liquid or a gas which kills microorganisms, or heat.

12. (Amended) Apparatus for separation of plasma from blood or from a buffy coat fraction [continuous purification and concentration of leukocytes, from blood], characterized in that said apparatus includes the following means:

(i) a membrane filter means for separating plasma from the blood by filtration in order to achieve a filtered buffy coat fraction;

(ii) a retention vessel [static mixer] means for mixing the buffy coat fraction and an aqueous hypotonic solution in order to achieve lysis [lysation] of erythrocytes contained in the buffy coat fraction;

(iii) a retention vessel means;

(iv) a centrifuge means in order to separate the leukocytes.

18. (Amended) Apparatus according to claim 11, characterized in that the centrifuge is adapted to continuous [or semi-continuous] separation of the leukocytes.